

# Occurrence, clinical manifestations, and prognosis of Guillain-Barré syndrome

H Rantala, M Uhari, M Niemelä

## Abstract

In order to obtain more information on the incidence of Guillain-Barré syndrome and recent developments in its prognosis, we analysed the severity and prognosis of Guillain-Barré syndrome in children diagnosed and treated during the years 1980-6 throughout Finland. The criteria for Guillain-Barré syndrome were fulfilled in 14 boys and 13 girls. The mean annual number of cases of Guillain-Barré syndrome was thus 3.9, giving a mean annual incidence of 0.38/100 000 of population under 15 years of age (95% confidence intervals 0.25 to 0.56/100 000). The incidence of Guillain-Barré syndrome causing permanent neurological defects in children under 15 years of age was 1.4/10 million annually (95% confidence intervals 0.035 to 7.8/10 million). Our figures appeared to be one fourth to a half of that reported earlier in children and even lower than those in adults. Although there were no deaths among our patients, mortality from Guillain-Barré syndrome seems to have remained similar for the last 20 years despite current awareness of the possibility of cardiac arrest and respiratory failure.

The overall annual incidence of the Guillain-Barré syndrome has been estimated to be 1.7/100 000 persons,<sup>1</sup> but no separate incidence figures are available for children. Similarly our knowledge of the impact of Guillain-Barré syndrome at the population level is incomplete. In general, reports concerning Guillain-Barré syndrome in children are based on patients treated in one referral hospital,<sup>1-8</sup> which may cause bias in assessments of the severity of Guillain-Barré syndrome, as the worst cases are most likely to be reported. On the other hand, its severity and prognosis in childhood have been evaluated in surveys involving patients treated mainly during 1960-70.<sup>1-7</sup> In these series mortality varied up to a maximum of 9%,<sup>6</sup> most of the deaths being caused by cardiac arrest or respiratory failure.<sup>8</sup> It may be that the awareness of these events and the better possibilities for treating such patients have improved the prognosis for Guillain-Barré syndrome during the last 10 years.

In order to obtain more information about the incidence of Guillain-Barré syndrome and recent developments in its prognosis, we analysed its severity and prognosis in children, reviewing the literature and the records of patients diagnosed and treated during the years 1980-6 over the whole of Finland.

## Patients and methods

### SOURCES OF DATA

The Finnish National Board of Health keeps a central database on the diagnosis, sex, and age of the patients discharged from all the hospitals in the country. Patients discharged during the period from 1 January 1980 to 31 December 1986 from paediatric wards with a diagnosis of any kind of polyneuropathy were listed and their case histories reviewed by us. The mean population at risk in Finland during 1980-6 was 1.02 million.

### CRITERIA FOR GUILLAIN-BARRÉ SYNDROME

The findings listed by the Guillain-Barré syndrome study group were used as criteria (table 1).<sup>9</sup> The case histories of 83 children were reviewed by a paediatric neurologist (HR) and 14 boys and 13 girls were found to fulfil the criteria.

### STATISTICAL METHODS

The occurrence of cases of Guillain-Barré syndrome was assumed to follow an even distribution in time and place. Confidence intervals were calculated based on a Poisson distribution.

## Results

The mean annual number of cases of Guillain-Barré syndrome was 3.9, giving a mean annual incidence of 0.38/100 000 of population under 15 years of age (95% confidence intervals 0.25 to 0.56/100 000). The incidence of Guillain-Barré syndrome causing permanent neurological defects in children under 15 years of age was 1.4/10 million annually (95% confidence intervals 0.035 to 7.8/10 million). The patients were evenly distributed in terms of age, which varied between 0.4 and 14.3 years. A preceding infection was verified in 23 patients with respiratory symptoms occurring most frequently (n=18). A vaccination before the symptoms was recorded in 11 patients.

The disease began from the lower extremities in 25 patients, one had paresis of the urinary bladder as the first sign of the disease, and one had paraesthesia (table 1). Nine had facial palsy, three had paresis of the abducens nerve, one had a bilateral hypoglossus paresis, and two had bulbar paresis. Twenty children had pain in the back or in the lower extremities two to 14 days before the onset of the neurological defects. Four children had meningism. An increase in blood pressure requiring medical treatment was found in one patient.

Department of  
Paediatrics,  
University of Oulu,  
SF-90220 Oulu,  
Finland

H Rantala  
M Uhari  
M Niemelä

Correspondence and requests  
for reprints to:  
Dr Uhari.

Accepted 1 February 1991

**Table 1** Diagnostic criteria for the Guillain-Barré syndrome as laid down by the Guillain-Barré syndrome study group,<sup>9</sup> and numbers of patients fulfilling the criteria in the present series

| Criteria   | No. of patients |
|--|-----------------|
| Features required for diagnosis:   |                 |
| Progressive motor weakness in more than one limb   | 27              |
| Areflexia or appreciable hyporeflexia  | 27              |
| Cerebrospinal fluid cell counts of no more than 50/mm <sup>3</sup> monocytes or 2/mm <sup>3</sup> polymorphonuclear leukocytes | 26*             |
| Features strongly supportive of the diagnosis:   |                 |
| Progression over some days to a few weeks  | 27              |
| Cranial nerve involvement  | 13              |
| Onset of recovery two to four weeks after half in progression  | 27              |
| Raised cerebrospinal fluid protein after one week of symptoms  | 26*             |
| Abnormal electrodiagnostics with slowed conduction or prolonged F waves  | 20              |

\*Lumbar puncture was not performed on one patient because of a suspicion of increased intracranial pressure.

A lumbar puncture was performed in all cases except one, where it was avoided because of a suspicion of increased intracranial pressure. Protein concentration in the cerebrospinal fluid was increased in all the patients (mean (SD) 1177 (774) mg/l). None had pleocytosis.

Five children needed assisted ventilation, all of whom received corticosteroids, and a plasmapheresis was performed on three of them. No one else received corticosteroids or plasmapheresis. The symptoms worsened over one to 33 days (mean 8.5 days), but none of the patients died. The duration of hospitalisation varied from four to 70 days (mean 34.1 days).

Eighteen children required physiotherapy for a period of three weeks to 22 months (mean 155 days) after discharge from hospital. All the children became symptomless in 22 days to 22 months (mean 158 days), except for one girl who still has a severe sensory neuropathy 5.5 years after the acute phase.

## Discussion

The annual incidence of Guillain-Barré syndrome in children under 15 years of age 0.38/100 000 is very low compared with that in adults. Kennedy *et al* found a lower incidence of Guillain-Barré syndrome among patients less than 40 years of age than in older ones, the incidence rates being 1.1 and 3.3/100 000 of population, respectively.<sup>1</sup> They did not give any separate incidence figures for children, however. Our figures are one fourth or a half of those reported in Western Australia, which were 1.13/100 000 in children of 0–9 years of age and of 0.62/100 000 in patients of 10–19 years of age.<sup>10</sup> The figures are not fully comparable, however, as the numbers of children under 15 years of age are not available from their data.<sup>10</sup>

Our study covered the whole population for seven years, during which there was a cluster of Guillain-Barré syndrome temporally associated with an oral polio vaccine campaign.<sup>11</sup> Thus our figures, if anything, are somewhat higher than the real incidence. The cases were collected starting with a loose initial diagnosis to ensure

that all cases were found. The heads of the paediatric wards in the country were aware that we were collecting cases of Guillain-Barré syndrome during 1980 to 1986 and this improved our coverage. Thus it is very unlikely that any significant number of cases were left unrecorded. Sometimes Guillain-Barré syndrome is difficult to diagnose, however, and those with a totally wrong diagnosis or a mild clinical symptomatology with myalgia and temporal muscular weakness could have been left out of our survey.

Although the acute symptoms were severe in most cases, the outcome was good. The symptoms of Guillain-Barré syndrome did not differ significantly from those in earlier reports,<sup>1–8</sup> but the great number of children with severe muscle pain was striking and caused differential diagnostic difficulties. There was no mortality, and the incidence of late sequelae was only 1.4/10 million children under 15 years of age. Earlier reports have mentioned mortality due to cardiac arrest or respiratory insufficiency because of either bulbar paresis or paresis of the respiratory muscles.<sup>6,8</sup> Cole and Matthew emphasised the importance of the possibility of aspiration, which may unexpectedly precipitate the need for mechanical ventilation.<sup>8</sup> Oral feeding should be avoided in the presence of bulbar involvement and poor respiratory function. Fluid balance should be ensured by intravenous infusion whenever there is any indication of autonomic disturbances and whenever oral feeding has been denied. Pulmonary collapse or consolidation was not a problem in our patients, which may indicate that the doctors were aware of the dangers of oral feeding in cases of Guillain-Barré syndrome. None of our patients had cardiac involvement, nor were reports found of cardiac arrhythmias treated with a pacemaker. The use of artificial pacing might nevertheless be one important improvement achieved in the treatment of Guillain-Barré syndrome.

The five children with the most severe symptoms in our survey needed assisted ventilation and received corticosteroids, and plasmapheresis was also performed on three of them. All returned to full health without any sequelae. The prognosis cannot be predicted on the basis of the severity of the acute phase.<sup>8</sup> There is no evidence of corticosteroids being effective.<sup>12</sup> In the controlled trials of plasmapheresis in adults it has been found to be either ineffective or to have shortened the duration of severe weakness and assisted ventilation, but no effect has been reported on the mortality.<sup>9,13,14</sup> The experience of plasmapheresis in Guillain-Barré syndrome in children is limited. Khatri *et al* reported good clinical responses in their uncontrolled series of 11 children with Guillain-Barré syndrome.<sup>15</sup> If plasmapheresis is to be used it should be employed in the early phase of the disease and by those who have experience with intensive plasmapheresis in paediatric patients.<sup>15</sup> Recently it has been reported that intravenously administered immune serum globulin may be beneficial in childhood Guillain-Barré syndrome.<sup>16</sup>

No temporal trend in the prognosis was found in the combined data on Guillain-Barré

Table 2 Prognosis for Guillain-Barré syndrome in different studies

| Authors                            | Time    | No of patients | Selection  | No (%) of deaths | Assisted ventilation |
|------------------------------------|---------|----------------|------------|------------------|----------------------|
| Markland and Riley <sup>5</sup>    | 1951-63 | 19             | Hospital   | 0                | —                    |
| Paulson <sup>6</sup>               | 1961-8  | 46             | Hospital   | 4 (9)            | 11                   |
| Briscoe <i>et al</i> <sup>17</sup> | 1970-85 | 24             | Hospital   | 1 (4)            | 1                    |
| Evans <sup>18</sup>                | 1971-7  | 18             | Hospital   | 0                | 2                    |
| Hogg <i>et al</i> <sup>19</sup>    | 1972-6  | 5              | Population | 1 (20)           | 1                    |
| Kleyweg <i>et al</i> <sup>20</sup> | 1975-87 | 18             | Hospital   | 2 (11)           | 4                    |
| Cole and Matthew <sup>8</sup>      | 1977-84 | 11             | Hospital*  | 2 (18)           | 11                   |
| Present series                     | 1980-6  | 27             | Population | 0                | 5                    |
| Combined                           |         | 168            |            | 10 (5.9)         | 35                   |

\*Only those needing assisted ventilation were included.

syndrome in children (table 2). Although we found no mortality, our survey did not significantly differ from those reported earlier. The frequency of the need for assisted ventilation of 5/27 is a common figure, indicating that our patients represent a typical series of cases of Guillain-Barré syndrome despite being based on a nationwide survey.

Although Guillain-Barré syndrome is a rare disease with a relatively good long term outcome, it causes a long period of hospitalisation and a prolonged need for rehabilitation. The Guillain-Barré syndrome is still a serious and sometimes life threatening condition.

This research was supported financially by the Paulo Foundation, Helsinki, Finland.

## Commentary

Rantala and colleagues report an age specific annual incidence of 0.38/100 000. Similar figures have been reported from Denmark,<sup>1</sup> Norway,<sup>2</sup> and the USA.<sup>3</sup> The last mentioned study reported a linear increase in incidence with increasing age throughout childhood and adult life. These reports, however, can only describe the course of the condition in cases in whom the correct diagnosis is made.

Hospital based reports have emphasised the difficulties of diagnosis, especially in children. Three of the last five personal cases have been referred for the first time after cardiac arrest and still bearing other diagnoses. Of the remaining two, one had been misdiagnosed as encephalitis and the other had prominent pain and cramps, preserved reflexes and reasonable preservation of power at the time when cerebrospinal fluid examination and neurophysiology confirmed the diagnosis.

The classical signs of limb weakness and hyporeflexia may be unimpressive early in the illness. Again, abnormalities of cerebrospinal fluid protein and nerve conduction velocity may not be striking early in the illness. The Guillain-Barré study group listed,<sup>4</sup> in addition to those features tabulated by Rantala *et al*, the following other clinical features strongly supportive of the diagnosis: mild sensory signs or symptoms, autonomic dysfunction, initial absence of fever, and relative symmetry of impairment. The diagnosis should be considered in any child with acute or subacute unexplained ataxia, cranial nerve palsies, weakness or pain in the trunk and/or limbs. Patients with Guillain-Barré syndrome may be misdiagnosed as having encephalitis (which may also accompany the Guillain-Barré syndrome), myositis, cachexia, arthralgia, arthritis, transverse myelitis, behaviour disorder, or hysteria. Prominent cranial nerve involvement may lead to an apparent absence of brainstem reflexes and be misinterpreted as coma, particularly if accompanied by limb paralysis. The Miller-Fisher variant may present with cranial nerve involvement ataxia and proprioceptive loss without detectable motor weakness.

The differential diagnosis of subacute polyneuropathy includes glue sniffing, diphtheria, botulism, heavy metal poisoning, poliomyelitis, organophosphate poisoning, myasthenia gravis (tick paralysis), and rabies.

The series of Rantala *et al* is similar to others in reporting the need for assisted ventilation

- Kennedy RH, Danielson MA, Mulder DW, Kurland LT. Guillain-Barré syndrome. A 42-year epidemiologic and clinical study. *Mayo Clin Proc* 1978;53:93-9.
- Casamajor L, Alpert GR. Guillain-Barré-Strohl syndrome in children. *Am J Dis Child* 1941;61:99-107.
- Low NL, Schneider J, Carter S. Polyneuritis in children. *Pediatrics* 1958;22:972-90.
- Peterman AF, Daly DD, Dion FR, Keith HM. Infectious neuritis (Guillain-Barré-Strohl syndrome) in children. *Neurology* 1959;9:533-9.
- Markland LD, Riley HD. The Guillain-Barré syndrome in childhood. *Clin Pediatr (Phila)* 1967;6:162-70.
- Paulson GW. The Landry-Guillain-Barré-Strohl syndrome in childhood. *Dev Med Child Neurol* 1970;12:604-7.
- Rossi LN, Mumenthaler M, Lutschg J, Ludin HP. Guillain-Barré syndrome in children with special reference to the natural history of 38 personal cases. *Neuropediatrics* 1976;7:42-51.
- Cole GF, Matthew DJ. Prognosis in severe Guillain-Barré syndrome. *Arch Dis Child* 1987;62:288-91.
- The Guillain-Barré Syndrome Study Group. Plasmapheresis and acute Guillain-Barré syndrome. *Neurology* 1985;35:1096-104.
- Hankey GJ. Guillain-Barré syndrome in Western Australia, 1980-1985. *Med J Austr* 1987;146:130-3.
- Uhari M, Rantala H, Niemelä M. Cluster of childhood Guillain-Barré cases after an oral polio vaccine campaign. *Lancet* 1989;ii:440-1.
- Hughes RAC, Newsom-Davis JM, Perkins GD. Controlled trial of prednisolone in acute polyneuropathy. *Lancet* 1978;ii:750-3.
- Greenwood RJ, Newsom-Davis J, Hughes RAC, *et al*. Controlled trial of plasma exchange in acute inflammatory polyradiculoneuropathy. *Lancet* 1984;ii:877-9.
- Osterman PG, Fagius J, Lundemo G, *et al*. Beneficial effects of plasma exchange in acute inflammatory polyradiculoneuropathy. *Lancet* 1984;ii:1296-9.
- Khatiri BO, Flamini JR, Baruah JK, Dobyns WB, Konkol RJ. Plasmapheresis with acute inflammatory polyneuropathy. *Pediatric Neurology* 1990;6:17-9.
- Shahar E, Murphy EG, Roifman CM. Benefit of intravenously administered immune serum globulin in patients with Guillain-Barré syndrome. *J Pediatr* 1990;116:141-4.
- Briscoe DM, McMenamin JB, O'Donohoe NV. Prognosis in Guillain-Barré syndrome. *Arch Dis Child* 1987;62:733-5.
- Evans OB. Polyneuropathy in childhood. *Pediatrics* 1979;64:96-105.
- Hogg JE, Kobrin DE, Schoenberg BS. The Guillain-Barré syndrome epidemiologic and clinical features. *J Chronic Dis* 1979;32:227-31.
- Kleyweg RP, van der Meché FG, Loonen MCB, de Jonge J, Knip B. The natural history of the Guillain-Barré syndrome in 18 children and 50 adults. *J Neurol Neurosurg Psychiatry* 1989;52:853-6.